

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising at least one Kunitz domain that comprises an amino acid sequence according to the formula Cys Xaa2 Xaa3 Xaa4 Xaa5
5 Xaa6 Xaa7 Xaa8 Xaa9 Cys Xaa11 Xaa12 Xaa13 Xaa14 Xaa15 Xaa16 Xaa17 Xaa18 Xaa19
Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Xaa25 Cys Xaa27 Xaa28 Phe Xaa30 Xaa31 Xaa32 Gly
Cys Xaa35 Xaa36 Xaa37 Xaa38 Asn Xaa40 Xaa41 Xaa42 Xaa43 Xaa44 Xaa45 Xaa46 Cys
Xaa48 Xaa49 Xaa50 Cys (SEQ ID NO:2), wherein the amino acid sequence is at least about
80% identical to the sequence of residues 5-55 of SEQ ID NO:1.
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2. The polypeptide of claim 1, wherein the amino acid sequence is characterized by one or more of the following conditions: Xaa2 is an Ala, Val, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Phe, Tyr, or Met residue, or is absent; Xaa3 is an Ala, Val, Leu, Ser, Thr, Asp, Glu, Gln, Phe, or Met residue, or is absent; Xaa4 is a Gly, Ala, Leu, Ser, Asp, Lys,
15 Glu, Gln, or Pro residue, or is absent; Xaa5 is Ala, Val, Leu, Glu, Ser, Asn, Lys, Glu, Tyr, Met, Pro, or is absent; Xaa6 is an Ala, Val, Leu, Ser, Asp, Asn, Lys, Glu, Arg, Tyr, or Met residue, or is absent; Xaa7 is an Ala, Val, Thr, Asp, Lys, Glu, Gln, Arg, His, Tyr, or Pro residue, or is absent; Xaa8 is a Gly or Asp residue, or is absent; Xaa9 is a Leu, Glu, Ser, Thr, Asn, Gln, Arg, or Pro residue, or is absent; Xaa11 is a Gly, Ala, Leu, Ser, Thr, Asn, Lys, Glu,
20 Gln, Arg, or Met residue, or is absent; Xaa12 is a Gly, Ala, Thr, Asp, Glu, or His residue, or is absent; Xaa13 is a Leu, Glu, Ser, Asn, Glu, Arg, Phe, Trp, Tyr, or Met residue, or is absent; Xaa14 is an Ala, Val, Leu, Glu, Thr, Glu, Phe, or Met residue, or is absent; Xaa15 is an Ala, Val, Leu, Glu, Ser, Thr, Asn, Lys, Glu, Gln, or Pro residue, or is absent; Xaa16 is a Leu, Lys, Arg, or His residue, or is absent; Xaa17 is a Phe, Trp, or Tyr residue, or is absent; Xaa18 is
25 an Ala, His, Phe, Trp, or Tyr residue, or is absent; Xaa19 is a Phe or Tyr residue, or is absent; Xaa20 is a Val, Ser, Asp, Asn, or Arg residue, or is absent; Xaa21 is a Gly, Ala, Leu, Glu, Ser, Asn, Lys, Phe, or Pro residue, or is absent; Xaa22 is a Val, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Phe, or Tyr residue, or is absent; Xaa23 is an Ala, Val, Leu, Glu, Ser, Thr, Asp, Asn, Lys, Glu, Arg, or Tyr residue, or is absent; Xaa24 is a Gly, Asn, Lys, Glu, Gln, Arg, Tyr,
30 or Met residue, or is absent; Xaa25 is an Ala, Leu, Glu, Ser, Thr, Lys, Glu, Gln, Arg, or His residue, or is absent; Xaa27 is an Ala, Val, Ser, Thr, Asp, Asn, Lys, Glu, Gln, Arg, or His residue, or is absent; Xaa28 is an Ala, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Met, or Pro residue, or is absent; Xaa30 is an Ala, Val, Leu, Glu, Thr, Lys, Gln, Phe, Trp, or Pro residue, or is absent; Xaa31 is a Ser, Phe, or Tyr residue, or is absent; Xaa32 is a Gly, Ser, Thr, or
35 Arg residue, or is absent; Xaa35 is a Gly, Leu, Asp, Asn, Glu, Gln, Arg, His, Tyr, or Met residue, or is absent; Xaa36 is a Gly, Ala, or Arg residue, or is absent; Xaa37 is a Ser, Asp,

Asn, or Lys residue, or is absent; Xaa38 is a Gly, Ala, Ser, Asp, Asn, Lys, Glu, Gln, or Arg residue, or is absent; Xaa40 is a Ser, Asn, Lys, or Arg residue, or is absent; Xaa41 is a Phe or Tyr residue, or is absent; Xaa42 is a Gly, Ala, Val, Leu, Thr, Asp, Asn, Lys, Glu, Gln, Arg, His, Tyr, or Pro residue, or is absent; Xaa43 is a Ser, Thr, Asp, Asn, Glu, or Arg residue, or is absent; Xaa44 is an Ala, Leu, Lys, Glu, Gln, Arg, or Trp residue, or is absent; Xaa45 is an Ala, Asp, Lys, Glu, or Gln residue, or is absent; Xaa46 is an Ala, Ser, Thr, Asp, Asn, Lys, Glu, Gln, or Tyr residue, or is absent; Xaa48 is a Leu, Ile, Glu, Asp, Lys, Glu, Gln, Arg, or Met residue, or is absent; Xaa49 is a Gly, Ala, Leu, Ser, Thr, Asp, Asn, Lys, Glu, Gln, or Arg residue, or is absent; and Xaa50 is an Ala, Ser, Thr, Val, Glu, Lys, Arg, Phe, or Met residue, or is absent.

3. The isolated polypeptide according to claim 2, wherein Xaa2 is an Ala, Val, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Phe, Tyr, or Met residue, or is absent; Xaa3 is an Ala, Val, Leu, Ser, Thr, Asp, Glu, Gln, Phe, or Met residue, or is absent; Xaa4 is a Gly, Ala, Leu, Ser, Asp, Lys, Glu, Gln, or Pro residue, or is absent; Xaa5 is Ala, Val, Leu, Glu, Ser, Asn, Lys, Glu, Tyr, Met, Pro, or is absent; Xaa6 is an Ala, Val, Leu, Ser, Asp, Asn, Lys, Glu, Arg, Tyr, or Met residue, or is absent; Xaa7 is an Ala, Val, Thr, Asp, Lys, Glu, Gln, Arg, His, Tyr, or Pro residue, or is absent; Xaa8 is a Gly or Asp residue, or is absent; Xaa9 is a Leu, Glu, Ser, Thr, Asn, Gln, Arg, or Pro residue, or is absent; Xaa11 is a Gly, Ala, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, or Met residue, or is absent; Xaa12 is a Gly, Ala, Thr, Asp, Glu, or His residue, or is absent; Xaa13 is a Leu, Glu, Ser, Asn, Glu, Arg, Phe, Trp, Tyr, or Met residue, or is absent; Xaa14 is an Ala, Val, Leu, Glu, Thr, Glu, Phe, or Met residue, or is absent; Xaa15 is an Ala, Val, Leu, Glu, Ser, Thr, Asn, Lys, Glu, Gln, or Pro residue, or is absent; Xaa16 is a Leu, Lys, Arg, or His residue, or is absent; Xaa17 is a Phe, Trp, or Tyr residue, or is absent; Xaa18 is an Ala, His, Phe, Trp, or Tyr residue, or is absent; Xaa19 is a Phe or Tyr residue, or is absent; Xaa20 is a Val, Ser, Asp, Asn, or Arg residue, or is absent; Xaa21 is a Gly, Ala, Leu, Glu, Ser, Asn, Lys, Phe, or Pro residue, or is absent; Xaa22 is a Val, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Phe, or Tyr residue, or is absent; Xaa23 is an Ala, Val, Leu, Glu, Ser, Thr, Asp, Asn, Lys, Glu, Arg, or Tyr residue, or is absent; Xaa24 is a Gly, Asn, Lys, Glu, Gln, Arg, Tyr, or Met residue, or is absent; Xaa25 is an Ala, Leu, Glu, Ser, Thr, Lys, Glu, Gln, Arg, or His residue, or is absent; Xaa27 is an Ala, Val, Ser, Thr, Asp, Asn, Lys, Glu, Gln, Arg, or His residue, or is absent; Xaa28 is an Ala, Leu, Ser, Thr, Asn, Lys, Glu, Gln, Arg, Met, or Pro residue, or is absent; Xaa30 is an Ala, Val, Leu, Glu, Thr, Lys, Gln, Phe, Trp, or Pro residue, or is absent; Xaa31 is a Ser, Phe, or Tyr residue, or is absent; Xaa32 is a Gly, Ser, Thr, or Arg residue, or is absent; Xaa35 is a Gly, Leu, Asp, Asn, Glu, Gln, Arg, His, Tyr, or Met residue, or is absent; Xaa36 is a Gly, Ala, or Arg residue, or is absent; Xaa37 is a Ser,

Asp, Asn, or Lys residue, or is absent; Xaa38 is a Gly, Ala, Ser, Asp, Asn, Lys, Glu, Gln, or Arg residue, or is absent; Xaa40 is a Ser, Asn, Lys, or Arg residue, or is absent; Xaa41 is a Phe or Tyr residue, or is absent; Xaa42 is a Gly, Ala, Val, Leu, Thr, Asp, Asn, Lys, Glu, Gln, Arg, His, Tyr, or Pro residue, or is absent; Xaa43 is a Ser, Thr, Asp, Asn, Glu, or Arg residue, or is absent; Xaa44 is an Ala, Leu, Lys, Glu, Gln, Arg, or Trp residue, or is absent; Xaa45 is an Ala, Asp, Lys, Glu, or Gln residue, or is absent; Xaa46 is an Ala, Ser, Thr, Asp, Asn, Lys, Glu, Gln, or Tyr residue, or is absent; Xaa48 is a Leu, Ile, Glu, Asp, Lys, Glu, Gln, Arg, or Met residue, or is absent; Xaa49 is a Gly, Ala, Leu, Ser, Thr, Asp, Asn, Lys, Glu, Gln, or Arg residue, or is absent; and Xaa50 is an Ala, Ser, Thr, Val, Glu, Lys, Arg, Phe, or Met residue, or is absent.

4. The isolated polypeptide of claim 3, wherein the polypeptide detectably inhibits the activity of at least one of the proteases selected from the group consisting of chymotrypsin, elastase, cathepsin G, proteinase 3, plasmin, plasma kallikrein, glandular kallikrein and trypsin.

5. The isolated polypeptide of claim 3, wherein the polypeptide is from 51 to about 80 amino acid residues in length.

6. The isolated polypeptide of claim 5, wherein the polypeptide is from 51 to about 70 residues in length.

7. The isolated polypeptide of claim 3, wherein the amino acid sequence is characterized by one or more of the following Xaa5 is Pro; Xaa7 is Thr; Xaa9 is Pro; Xaa11 is Arg or Lys; Xaa12 of SEQ ID NO:2 is Ala; Xaa13 of SEQ ID NO:2 is Arg; Xaa14 of SEQ ID NO:2 is Ile; Xaa15 of SEQ ID NO:2 is Ile; Xaa30 of SEQ ID NO:2 is Val; and Xaa35 of SEQ ID NO:2 is Arg.

8. The isolated polypeptide of claim 7, wherein Xaa5 is Pro; Xaa7 is Thr; Xaa9 is Pro; Xaa11 is Arg or Lys; Xaa12 of SEQ ID NO:2 is Ala; Xaa13 of SEQ ID NO:2 is Arg; Xaa14 of SEQ ID NO:2 is Ile; Xaa15 of SEQ ID NO:2 is Ile; Xaa30 of SEQ ID NO:2 is Val; and Xaa35 of SEQ ID NO:2 is Arg.

9. The isolated polypeptide of claim 1, wherein the amino acid sequence comprises residues 5-55 of SEQ ID NO:1.

10. The isolated polypeptide of claim 9, wherein the amino acid sequence comprises residues 1-58 of SEQ ID NO:1.
11. The isolated polypeptide of claim 1, wherein the amino acid sequence
5 comprises SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or SEQ ID NO:7.
12. A nucleic acid encoding the polypeptide of claim 3.
13. A vector comprising the nucleic acid of claim 12.
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14. A host cell comprising the nucleic acid of claim 12.
15. A composition comprising the polypeptide of claim 1 and a
pharmaceutically acceptable carrier, vehicle, diluent, excipient, or a combination of any
15 thereof.
16. A composition comprising the polypeptide of claim 3 and a
pharmaceutically acceptable carrier, vehicle, diluent, excipient, or a combination of any
thereof.
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17. A composition comprising the polypeptide of claim 9 and a
pharmaceutically acceptable carrier, vehicle, diluent, excipient, or a combination of any
thereof.
18. A method for inducing, promoting, and/or enhancing at least one
25 physiological response associated with the treatment or prevention of systemic inflammatory
response syndrome, acute pancreatitis, shock syndrome, hyperfibrinolytic hemorrhage, or
myocardial infarction or for preventing blood loss in a subject comprising administering the
composition of claim 15 to the subject in an amount sufficient to induce, promote, and/or
30 enhance the physiological response.
19. A method for inducing, promoting, and/or enhancing at least one
physiological response associated with the treatment or prevention of systemic inflammatory
response syndrome, acute pancreatitis, shock syndrome, hyperfibrinolytic hemorrhage, or
35 myocardial infarction or for preventing blood loss in a subject comprising administering the

composition of claim 16 to the subject in an amount sufficient to induce, promote, and/or enhance the physiological response.

20. A method for inducing, promoting, and/or enhancing at least one
5 physiological response associated with the treatment or prevention of systemic inflammatory response syndrome, acute pancreatitis, shock syndrome, hyperfibrinolytic hemorrhage, or myocardial infarction or for preventing blood loss in a subject comprising administering the composition of claim 17 to the subject in an amount sufficient to induce, promote, and/or enhance the physiological response.